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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/761,913	01/20/2004	Neil Moss	09-0216-1-D1	4313

28518 7590 06/30/2008

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EXAMINER	
PACKARD, BENJAMIN J	

ART UNIT	PAPER NUMBER
1612	

MAIL DATE	DELIVERY MODE
06/30/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/761,913	MOSS ET AL.	
	Examiner	Art Unit	
	Benjamin Packard	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 March 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6-13, 15-18, and 20-22* is/are rejected.

7)☒ Claim(s) *14,19 and 23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed 3/13/2008, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Status of the Claims

Claims 14, 19, and 23 are free of the prior art because the prior art does not disclose the instant group Q as a heterocyclic alkyl (or morpholine).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling inhibiting TNF-alpha in lipopolysaccharide stimulated THP cells, does not reasonably provide enablement for treating the broader cytokine-mediated cancers, acute myelogenous leukemia blasts, or plasma cell dyscrasias. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

To be enabling, the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated:

The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence or absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art,

7) the predictability of the art, and

8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. In re Fisher, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, all Wands factors have been considered and the following factors that are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill level

The invention relates to treatment of disease, particularly treating cancer. The relative skill of those in the art is high, that of an MD or PHD. That factor is outweighed, however, by the unpredictable nature of the art. As illustrative of the state of the art, the examiner cites Suggitt and Bibby, *Clinical Cancer Research*, 2005, Vol 11, 971-981. Suggitt and Bibby teaches the unpredictability of treating cancer. Note however, that the current human tumor cell line in vitro screen is generally unpredictable. Modern methods are susceptible to false-positive and false-negative results. (page 973 1st paragraph on right-hand column). Difficulty in determining results leads to difficulty in testing for effectiveness of compounds, which leads to unpredictability in treating cancers.

2. The breadth of the claims

The claim relates to treating various forms of cancer.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance for treatment of the many possible cancers. No reasonably specific guidance is provided concerning useful therapeutic protocols for disorders, other than inhibiting TNF-alpha in lipopolysaccharide stimulated THP cells. The latter is corroborated by the working examples.

4. The quantity of experimentation necessary

Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that the instantly claimed agents could be predictably used for treatment of the many possible cancers as inferred by the claim and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the invention claimed in the patent a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 and 6-21 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "-mediated" in claim 1, 16, and 20 is a relative term which renders the claim indefinite. The term "-meidated" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 6-13, 15-18, and 20-22 were rejected under 35 U.S.C. 103(a) as being unpatentable over Dumas et al. (WO 99/32110 as cited in the IDS) in view of Hanna (US 2002/0012665), Bruserud (Leukemia Research, 1996, Vol. 20, No. 1, pp. 65-73), and Treon et al. (Current Opinion in Hematology, 1998, Vol. 5, pp. 42-48).

This rejection is maintained.

The claims were rejected because Dumas et al., Bruserud, and Treon et al teach a method of treating cytokine mediated diseases in humans or mammals comprising administering a group of aryl ureas, which are the compounds of formula (I) and pharmaceutically acceptable salts of formula (I) (abstract; page 6, lines 26-27; and page 15, lines 1-2) useful for a number of cytokine mediated disease including cancer (page 7, lines 17 and 19), including acute myelogenous leukemia (page 3, paragraph [0030]).

Thus it would be obvious that Hanna teaches a method of treating acute myelogenous leukemia and multiple myeloma.

To a person of skill in the art at the time of the invention, it would have been obvious to employ the compounds of formula (I) of Dumas et al. to treat cytokine mediated cancers such as multiple myeloma and acute myelogenous leukemia because the compounds of Hanna, Bruserud, and Treon et al. are used for treating various cancers and tumors including multiple myeloma and acute myelogenous leukemia and according to Hanna and Bruserud, cytokine antagonists can be used to treat cytokine mediated cancers such as acute myelogenous leukemia and according to Treon et al., cytokine antagonists can be used to treat cytokine mediated cancers such as multiple myeloma.

Applicants' arguments

Applicants amended the claims to exclude Ar_2 as phenyl and suggest Dumas et al only exemplifies compounds where R^2 is phenyl. Further, Applicants state there is no suggestion to make any of the substitutions in order to arrive at the claimed compounds and doing so would require tenuous substitutions.

Examiner's Response

Examiner points out that the previous disclosure specifically discloses 2-substituted-5-tert-butylpyrazolyl ureas as the preferred core structure embodiment (see page 40 table 1). Therefore, the only picking and choosing required is for R^1 and R^2.

Also note that the R^1 groups suggested are generally substituted phenyl groups, where the substation is ortho, meta, and para, with groups such as methyl, amine, nitro,

and methoxy. Similarly, the suggested R^2 groups include phenyl groups para-substituted. Further, Claim 1 of Dumas et al teaches B as a substituted aryl (which is up to tricyclic), where it is substituted by X=-OR^5, when R^5 is an C_4-C_{23} alkheteroaryl.

The closest preferred embodiment disclosed is example 37 on page 43 when compared to 1-[5-tert-butyl-2-p-tolyl-2H-pyrazol-3-yl]-3-[4-(pyridin-4-yl-methoxy)naphthalen-1-yl]-urea of instant claim 12.

R1 differs only in that the phenyl group is substituted with a fluorine, rather than a methyl. It would have been obvious to one of ordinary skill in the art to use methyl in the para-position because methyl had been used in other positions for other embodiments, showing the functionality of the methyl in this group similar to that of the fluorine.

Note, instant claim 1 allows for halo substitution, therefore R1 read directly on the family of compounds of instant claim 1.

R2 is monocyclic phenyl substituted with a 4-methoxypyridinyl. The difference is the missing methene group and the dicyclic phenyl (or naphthalenyl).

First, the methene would be obvious to omit where the methene only serves to lengthen the hetero-chain between the two aromatic rings. Note, Instant claim 1 allows for Q to be pyridine, where L is a single methylene group replaced with O.

Second, it would have been obvious to use naphthalenyl instead of the phenyl B where they are structurally similar, both being aromatic carbon ring structures.

Therefore, even with the amended claims, it would have been obvious to one of ordinary skill in the art to make simple substitutions to one of the disclosed preferred embodiments to result in the instant compounds.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Benjamin Packard whose telephone number is 571-270-3440. The examiner can normally be reached on M-F 8-3:45 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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